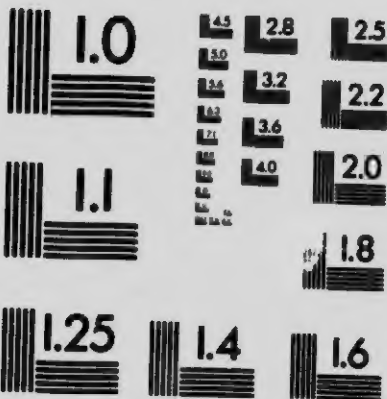


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in Prolonging Life, and in Alleviating
Distressing Symptoms

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THE VALUE OF RADIUM IN CURING DISEASE, IN PROLONGING LIFE, AND IN ALLEVIATING DISTRESSING SYMPTOMS*

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During the comparatively short time which has elapsed since radium was first introduced into therapeutics, the treatment has passed through many phases, but it is now being established upon a firm and scientific basis, and is slowly, but surely, extending enormously its field of usefulness. A few brilliant successes in its early days caused it to be hailed by over-enthusiastic advocates as an almost universal panacea; but, on the other hand, a certain number of failures resulted in its unconditional condemnation by some of the more conservative members of the profession, who are invariably inclined to be sceptical in regard to the merits of any new remedy. Further investigation and more extensive experience, however, have shown that for many of these failures radium itself was not to blame. The cause of failure might, almost invariably, be traced to a defective knowledge of its exact characteristics, dosage and method of application. In some instances also success did not result because of an injudicious selection of cases for treatment, for radium, in common with every other method, has its limitations. The absolute necessity of recognizing these, and giving them due consideration, before formulating a definite opinion as to the value of radium treatment, will be obvious. Meanwhile, though the value of new remedies can only be accurately determined by prolonged experience and observation, it is advisable to approach the subject with an open and unbiased mind, and we should not hesitate to avail ourselves of any method which may present itself for removing or alleviating the terrible suffering caused by the diseases with which humanity is liable to be affected. Everyone will agree that cancer is one of the most important of these diseases.

Lack of knowledge as to the proper dosage has been responsible for failure in not a few cases, where either too much or

*Read at the meeting of the American Radium Society, Atlantic City, June 9-13, 1919.

too little radium has been given. The use of too small an amount of radium may account for failure, as an inadequate dose is said to have the effect of stimulating a malignant growth instead of attaining the desired object—inhibition.

Whilst it is now generally recognized that radium is dependent for much of its efficiency upon the fact that in cancer it exerts a selective destructive influence upon the cells of the new growth, there is no doubt whatever that, to a certain extent, it also affects normal tissue destructively. The effects of radium upon the cancer cells are described in a recent editorial in the *Lancet* as follows:—"The cells become granular and break up, and sometimes vacuoles appear until absorption of the debris occurs, and after a time a shrunken cell membrane is all that remains of the formerly malignant cells. Then there appears new fibrous tissue, the amount varying in different cases, and thus, if a successful result is obtained, the malignant growth is replaced by a fibrous nodule, whilst in some cases the cure is so complete that no trace whatever is left of the malignant disease." This destructive influence is exerted on all forms of living tissue, but is decidedly greater on the pathological cells than on the healthy tissue. Caution is therefore necessary lest, when we increase the dose in the hope of increasing its power to destroy the cancer cells, we do so to such an extent that it has a disastrous effect on normal tissue. When a lesion is deeply situated increased dosage will, to a certain extent, compensate for its increased depth, but such an increase is necessarily limited by the necessity of stopping the dosage at the point at which normal tissue would be endangered. This makes it imperative that the principles of dosage should be definitely established, and its limitations and variations in individual cases thoroughly understood. The investigations which have been carried out in recent years have added greatly to our knowledge in this respect, have reduced the risks, and thus have extended widely the field of usefulness of radium therapy.

Darier and others are of the opinion that another factor which has sometimes led to the discredit of radium treatment is the fact that in dealing with cancer of the skin, the absolute necessity of making an accurate diagnosis of the particular variety of cancer present before proceeding to treat it with radium has not been sufficiently recognized. This is of importance, in view of the fact that all the varieties of cancer which affect the skin do not respond equally well to radium.

This applies especially to the squamous and spino-celled epithelioma, in which rapid involvement of the lymphatics and metastases occur, and which usually terminate fatally in less than two years. A-melanotic sarcoma originating in naevi is also not so amenable to radium. Malignant disease, the aetiology of which still remains more or less a mystery, holds a prominent position among the morbid conditions for which we have, for many years past, been anxiously seeking a remedy. It was one of the first, and is still one of the chief conditions for which radium is employed. In the early days its use was largely restricted to the more superficial forms, but its beneficial effects gradually led to its use in more deeply-situated cancerous growths, such as cancer of the uterus and other internal organs. The cases of this kind which were at first submitted to radium were, as a rule, those in very advanced stages of malignancy, in which surgery and all other measures had failed, and radium was applied only as a last resource when the patients were in a desperate condition. Under these circumstances it was obviously unfair to blame the remedy for its failure to bring about a cure, but in spite of this fact cases have been reported from time to time in which the local manifestations have disappeared and the life of the patient has been prolonged.

After the many vicissitudes through which radium therapy has passed since its first introduction into therapeutics, it may be said to occupy at the present time a firmly established position. In some conditions, notably cancer of the face, it may be regarded as the treatment of election, as it can be relied upon to bring about a complete and permanent cure in a very large proportion of cases, without leaving the disfiguring and contracted scars which so often result from surgery, and which so frequently are the site of the recurrence of the trouble. In such cases there is no other treatment which can compare with radium in the excellence of its cosmetic results. A further recommendation of radium in this connection is the ease and painlessness with which it can be applied.

The treatment of more deeply situated cancer has been attended with varying success, sometimes in desperate and inoperable cases with the most unexpected success. Whilst there is no doubt that a sufficiently extensive surgical operation, provided it is possible to remove all the cancer cells present, gives a fair prospect of recovery and freedom from recurrence, yet, if the disease is allowed to progress it reaches a stage when surgical removal is impossible. In these advanced cases, which

are hopeless from the point of view of surgery, radium has shown itself to be invaluable, and there now appears to be no doubt that it exerts a reliable influence upon many forms of malignant growth.

THE VALUE OF RADIUM IN CURING DISEASE.

Among the most brilliant results which have been obtained from radium from this point of view are those in cancer of the skin and mucous membranes. This applies especially to basal-celled epithelioma and rodent ulcer. Other types of epithelioma are more refractory, most notably the squamous-celled variety, those accompanied by peripheral lymphangitis, and those recurrent in a cicatrix. Owing to this it was believed a few years ago that such forms of cancer were incurable by radium, but it is now generally recognized that the reason for failure was insufficient dosage. The squamous-celled variety of epithelioma required three or four times as much radium as the basal-celled variety in order to completely eradicate the disease and thus make recurrence improbable.

One great advantage of radium over surgery is that it leaves supple skin, with very little scar formation, whereas after operation there is a contracted scar, which is frequently the site of recurrence, owing to the irritation to which it is constantly subjected. I have frequently noted a reappearance of the disease at the site of stitch wounds. The value of radium in this connection will be appreciated when we remember that one of the facts which are definitely established in regard to cancer is that irritation is an important factor in its etiology.

Radium also has a wide field of use in the disease of the skin and mucous membrane other than malignancy; so much so, that its employment by modern dermatologists is almost imperative. Benign tumor growths, such as moles, warts, papillomata, are removed by it, while in the treatment of disfiguring birthmarks, either port-wine stains or angiomas, it is the method of election, as its application is easy and painless and its cosmetic results are not attained by any other method.

In keloid, lupus erythematosus, tuberculosis of the skin in its various aspects, it is of the greatest value. Leucoplakia of the buccal mucosa or tongue, which is often the forerunner of malignancy, responds favorably to radium therapy.

A recent report of the London Radium Institute states that experience there tends to show that rodent ulcer can be cured with certainty by the application of radium, and, provided that a sufficient dose is given, does not recur.

In the treatment of cancer of the lip, both in early and advanced cases the results are equal or superior to those of surgery. More than 90 p.c. of the early cases have been permanently cured without residual deformity, and also a fair proportion of the advanced cases. When we compare the 90 p.c. of cures without recurrence with the results of surgery in this condition, the superiority of the radium treatment is obvious. The literature of the subject shows that radical operation at an early stage, when there is no obvious affection of the glands, is followed by recurrence in more than 50 p.c. of the cases, and if the glands are involved at the time of operation, in more than 90 p.c.

The value of radium in treating sarcomatous tumors of the skin and some growths more deeply seated is well established.

Another condition in which the success of radium has been so remarkable that it has come to be regarded as the method of election, is that of fibroids of the uterus. In uncomplicated cases, however severe, experience indicates that it can be relied upon to arrest hæmorrhage and discharge, bringing about amenorrhœa, and it will also cause shrinkage or complete disappearance of the tumor.

Cases treated as long ago as 1905, when radium therapy was in the experimental stage, have remained in good health, and in many large gynæcological clinics the use of radium has almost superseded operation in fibroids and certain forms of uterine hæmorrhage. The only exceptions made are in cases in which the diagnosis is doubtful, in those in which the fibroids are suppurating, and in those in which symptoms of pressure render operations imperative. An advantage of radium in these cases as compared with the X-rays, which are also successful in arresting hæmorrhage and bringing about amenorrhœa, is that radium can be brought into direct contact with the diseased uterus, while the influence of X-rays depends almost entirely upon their action upon the ovaries. In the presence of sub-mucous fibroids, associated with endometritis, radium arrests the hæmorrhage by a primary action upon the endometrium and a secondary effect upon the ovaries, but with the X-rays the reverse takes place, and as a result the symptoms of the menopause due to radium are much less than those due to the action of the X-rays. In cases which are inoperable owing to the severity of the hæmorrhage, radium will often arrest the hæmorrhage and thus render the condition operable.

As regards cancer of the uterus, the mortality after surgery has been very great, even with the best technique and in the hands of the most skilful surgeons. The general opinion is that operation should be performed in every operable case, but that the use of radium after operation will tend to prevent recurrence, and thus increase the percentage of cures. In some instances the use of radium in an operable case will render a radical operation possible. A very large proportion of these cases are already inoperable when they first come under the observation of the surgeon.

In the therapy of Grave's disease, or exophthalmic goitre, a judicious use of the radium rays will in many cases produce results which are nothing less than brilliant, when combined, of course, with the usual medical measures of rest, diet, medication, etc. Radium applied over the thyroid slows the rapid pulse, lessens the nervous excitement, causes a variable degree of shrinkage of the gland, and in numerous cases has rendered quite unnecessary the surgical operation which has been proposed as a last resort in treatment of diseased thyroids.

2. THE VALUE OF RADIUM IN PROLONGING LIFE.

Those who express unfavorable opinions as to the value of radium therapy frequently do not consider sufficiently the fact that a very large number of the cases submitted to its treatment are in the last stages of cancer, when the growth is so extensive that surgery is powerless, and the patient is so ill that the fatal termination of the disease is imminent. In these cases radium is only used as a last resource, and it has frequently done what no other known form of treatment is capable of doing. In cases of inoperable cancer in the uterus and other regions, radium often causes disappearance of the local manifestations, and in certain cases cure has been effected in an apparently hopeless case. Life may thereby be prolonged for months or even years, although the patient may succumb subsequently to metastasis in other parts of the body.

Post-operative radiation is now regarded as a most important part of radium therapeutics. Many cases of cancer of various forms have been reported, in which the patient has remained without recurrence for three or four years or more after the radium treatment, sometimes for such a long period that cure may be assumed. In other cases the growth may become so much reduced in size that a previously inoperable case may become operable. In the report of the London Radium Institute, issued at the end of 1918, it stated that between 1911

and 1914 a large number of cases were operated upon by surgeons of high standing, and the operations were so extensive that, in the opinion of the operators, recurrence was inevitable. After post-operative treatment with radium, recurrence took place in less than 20 per cent. of the cases, a result which is believed to be unequalled in the records of selected cases operated upon by surgeons of extensive experience.

When radium is applied over the enlarged spleen, it has a favorable influence in myelogenous leukæmia. It is a well-known fact that this is one of the most hopeless conditions in the whole domain of medicine, and the literature of the subject indicates that practically all cases terminate fatally, the acute in a few months, the chronic in from two to four years. Ordway, Peabody, Griffin and Clarkson have recently discussed the treatment of this condition by the application of radium. The reduction of the white count is most remarkable, especially in the acute cases, and the size of the spleen is greatly decreased. Many of the patients have been able to return to their occupations for a time at least. These writers consider that radium is the best remedy we have at present. Should splenectomy be considered necessary, Griffin has shown that the operative mortality would be considerably reduced if operation could be performed at a time when the spleen was comparatively small, freely movable, and the general condition good. The first splenectomy for myelogenous leukæmia was reported by Bryant in 1866, the patient dying about two hours after. From this time up to 1915, 51 cases were reported with an operative mortality of 86 p.c. Mayo and Balfour have reported their results in 18 cases which were treated by pre-operative radium at the Mayo clinic. The spleen was much reduced in size, the operation easily performed, and the only post-operative complication was a case of peritonitis. Eight of the cases remained alive from nine months to three years after the treatment.

It has been demonstrated experimentally that the blood, spleen, bone marrow and lymph nodes are normally the most sensitive organs in the body to the action of radium and the X-rays. A few hours after irradiation there is a destruction of the cells of the lymphoid tissue and spleen and there is also a disappearance of the bone marrow. In the bone marrow the cells most easily affected are the lymphocytes and non-granular myelocytes. This destructive effect is much more marked in the leukæmic than in the normal animal, and in some cases after six weeks' treatment the white count has fallen from

1,250,000 to 8,000. In view of these results, the possibility is suggested that if treatment is begun at a sufficiently early stage, and continued long enough, the spleen, bone marrow and lymphatics may be influenced so favorably that the excessive production of immature forms of leucocytes may be definitely and permanently inhibited.

Even in cases in which the general condition is extremely bad, the radium treatment may be followed by marked improvement and increase in strength and weight, and there may be remissions of longer or shorter duration. Though death may ultimately supervene, there is no question but that the treatment may prolong life for a number of years. It remains a question whether cure will ultimately be obtained by means of improved technique or by treatment at an earlier stage, but it must be conceded that results already obtained are sufficiently remarkable. In Hodgkin's disease there is also a marked general improvement and reduction in the size of the affected lymphatics, but in order to obtain that result it is necessary to persevere with the treatment.

3. THE VALUE OF RADIUM IN ALLEVIATING DISTRESSING SYMPTOMS.

While I do not wish to minimize the curative value of radium, nor its value in the prolongation of life, it must be admitted that in many cases the prolongation of life alone would be a doubtful blessing, owing to the distressing symptoms which render life a burden, not only to the patient himself, but often to those around him also. In this direction radium has conferred one of the greatest benefits upon humanity. Radium has frequently been proved superior to every other known form of treatment, in that it has been able to control successfully the unpleasant symptoms associated with the last stages of malignant diseases in cases where recovery was apparently hopeless. Thus it renders the last weeks or months of the patient's life tolerable and comparatively comfortable. In not a few of these desperate cases the local symptoms have completely disappeared, or the growth has diminished to such an extent that operation can be performed with a fair prospect of success.

All authorities are agreed that in many very advanced cases of cancer of the uterus, radium relieves the pain, reduces the discharge and hæmorrhage, and causes the disappearance of the unpleasant odor which is such a trial to the patient and her

friends. In addition to this, unexpected apparent cures have been reported in some of these cases, and in those not ultimately cured there is marked relief in the symptoms.

During the war radium has been used extensively in the treatment of wounds. It has been found most useful in dealing with vicious cicatrices of various kinds, when they are associated with painful symptoms due to inclusion of nerve fibres or trunks, or when they interfere with the mobility of joints. In such cases the application of radium has frequently led to the restoration of normal mobility, to loosening of tendinous and muscular adhesions, and also to resumption of the function of compressed nerves. It has also given great relief in cutaneous manifestations, which have been observed so often in connection with war wounds and which are very refractory to ordinary methods of treatment. These are most frequently due to the excessive use of strong antiseptics, such as tincture of iodine, and have as a rule responded well to radium therapy. Degrais and Bellot report a series of excellent results in functional impairment following war wounds. They state that in vicious cicatrices radium acts in four ways: firstly, it transforms the cicatricial tissue into supple connective tissue; secondly, it dissolves and levels keloid tissue; thirdly, it detaches the cicatrix from adherent deep tissues; and lastly, it liberates compressed nerve fibres, causing disappearance or amelioration of motor or sensory troubles.

There is no doubt that the present position of radium therapy is very encouraging, and such as to give rise to great hopes for the future. There is no question as to its value as an adjunct to surgery, both before and after operations, and the results of prolonged experience leave no excuse for ignoring its usefulness in this connection. But perhaps the greatest benefit it has conferred upon humanity consists in the relief it has afforded to countless patients whose condition is absolutely hopeless from the point of view of cure. Even if it had never succeeded in curing a single case, radium has amply justified itself by its palliative properties.

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